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         AUG 06
                 FSTA enhanced with new thesaurus edition
         AUG 13
NEWS
                 CA/CAplus enhanced with additional kind codes for granted
                 patents
NEWS
         AUG 20
                 CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS
         AUG 27
                 Full-text patent databases enhanced with predefined
                 patent family display formats from INPADOCDB
         AUG 27
NEWS
                 USPATOLD now available on STN
NEWS
         AUG 28
                 CAS REGISTRY enhanced with additional experimental
                 spectral property data
NEWS
         SEP 07
                 STN AnaVist, Version 2.0, now available with Derwent
                 World Patents Index
         SEP 13
NEWS 10
                 FORIS renamed to SOFIS
         SEP 13
NEWS 11
                 INPADOCDB enhanced with monthly SDI frequency
NEWS 12
         SEP 17
                 CA/CAplus enhanced with printed CA page images from
                 1967-1998
NEWS 13
         SEP 17
                 CAplus coverage extended to include traditional medicine
                 patents
NEWS 14 SEP 24
                 EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS 15
         OCT 02
                 CA/CAplus enhanced with pre-1907 records from Chemisches
                 Zentralblatt
NEWS 16 OCT 19
                 BEILSTEIN updated with new compounds
NEWS 17
         NOV 15 Derwent Indian patent publication number format enhanced
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NEWS 19 NOV 30 ICSD reloaded with enhancements
NEWS 20 DEC 04 LINPADOCDB now available on STN
NEWS 21 DEC 14 BEILSTEIN pricing structure to change
NEWS 22 DEC 17 USPATOLD added to additional database clusters
NEWS 23
         DEC 17
                 IMSDRUGCONF removed from database clusters and STN
NEWS 24 DEC 17
                 DGENE now includes more than 10 million sequences
                 TOXCENTER enhanced with 2008 MeSH vocabulary in
NEWS 25
         DEC 17
                 MEDLINE segment
NEWS 26
         DEC 17
                 MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27
         DEC 17
                 CA/CAplus enhanced with new custom IPC display formats
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         DEC 17
                 STN Viewer enhanced with full-text patent content
                 from USPATOLD
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         JAN 02
                 STN pricing information for 2008 now available
NEWS 30
         JAN 16
                 CAS patent coverage enhanced to include exemplified
                 prophetic substances
NEWS 31
         JAN 28
                 USPATFULL, USPAT2, and USPATOLD enhanced with new
                 custom IPC display formats
NEWS 32
         JAN 28
                 MARPAT searching enhanced
NEWS 33
         JAN 28
                 USGENE now provides USPTO sequence data within 3 days
                 of publication
NEWS 34
         JAN 28
                 TOXCENTER enhanced with reloaded MEDLINE segment
```

NEWS 35 JAN 28 MEDLINE and LMEDLINE reloaded with enhancements NEWS 36 FEB 08 STN Express, Version 8.3, now available

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 24 JANUARY 2008

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http://www.cas.org/support/stngen/stndoc/properties.html

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=> E "N-HEXANOYL-D-SPHINGOSINE"/CN 25
            1 N-HEXANOYL-D-ERYTHRO-SPHINGOSINE/CN
E1
Ε2
            1
                 N-HEXANOYL-D-GLUCOSAMINE/CN
E3
            0 --> N-HEXANOYL-D-SPHINGOSINE/CN
E4
            1 N-HEXANOYL-DL-ALANINE/CN
E5
            1
                N-HEXANOYL-DL-GLUFOSINATE/CN
            1
E.6
                N-HEXANOYL-DL-METHIONINE/CN
E7
            1
                N-HEXANOYL-L-HOMOSERINE LACTONE/CN
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E.9
                  N-HEXANOYL-L-PHENYLALANINE/CN
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E10
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E22
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E23
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E25
            1
                  N-HEXANOYLHEPARIN/CN
=> S E1
T.1
             1 N-HEXANOYL-D-ERYTHRO-SPHINGOSINE/CN
=> DIS L1 1 SOIDE
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2008 ACS on STN
     124753-97-5 REGISTRY
     Hexanamide, N-[(1S,2R,3E)-2-hydroxy-1-(hydroxymethyl)-3-heptadecen-1-yl]-
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
    Hexanamide, N-[(1S,2R,3E)-2-hydroxy-1-(hydroxymethyl)-3-heptadecenyl]-
CN
     Hexanamide, N-[2-hydroxy-1-(hydroxymethyl)-3-heptadecenyl]-,
CN
    [R-[R*,S*-(E)]]-
OTHER NAMES:
    C6-Ceramide
CN
CN
    D-erythro-C6-Ceramide
CN
    N-Caproyl-C18-sphingosine
CN
    N-Hexanoyl-D-erythro-sphingosine
CN
    N-Hexanovlsphingosine
FS
    STEREOSEARCH
    C24 H47 N O3
MF
SR
    CA
LC
     STN Files:
                  AGRICOLA, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CIN,
       CSCHEM, TOXCENTER, USPAT2, USPATFULL
DT.CA CAplus document type: Journal; Patent
      Roles from patents: ANST (Analytical study); BIOL (Biological study);
RL.P
       PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
       reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological
       study); PREP (Preparation); PRP (Properties); USES (Uses)
RL.NP
      Roles from non-patents: ANST (Analytical study); BIOL (Biological
       study); CMBI (Combinatorial study); FORM (Formation, nonpreparative);
       OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties);
       RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: BIOL (Biological
       study)
```

Absolute stereochemistry.
Double bond geometry as shown.

Me
$$(CH_2)_4$$
 NH $(CH_2)_{12}$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

222 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

222 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file medline caplus wpids uspatfull

COST IN U.S. DOLLARS SINCE FILE TOTAL

FULL ESTIMATED COST ENTRY SESSION 8.07 8.28

FILE 'MEDLINE' ENTERED AT 10:18:02 ON 12 FEB 2008

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FILE 'USPATFULL' ENTERED AT 10:18:02 ON 12 FEB 2008

CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> s 11

L2 240 L1

=> s 12 and (paclitaxel or taxol)

L3 15 L2 AND (PACLITAXEL OR TAXOL)

=> d 13 1-15 ibib, abs

L3 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1420210 CAPLUS

DOCUMENT NUMBER: 148:24415

TITLE: ceramide and oxaliplatin combination for cancer

therapy

INVENTOR(S):
Wanebo, Harold J.

PATENT ASSIGNEE(S): Roger Williams Hospital, USA

SOURCE: PCT Int. Appl., 50pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

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WO 2007143175
                          А3
                                20080131
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA,
             CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI,
             GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,
             MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL,
             PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW,
             GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA
                         A1 20080207 US 2007-809418
     US 2008033039
                                                                    20070531
PRIORITY APPLN. INFO.:
                                            US 2006-810243P
                                                                P 20060602
     This invention provides a method for increasing apoptosis in a cancer cell
     comprising contacting the cancer cell with (a) oxaliplatin and (b)
     C6-ceramide, sequentially or concomitantly, wherein the oxaliplatin and
     C6-ceramide are in amts. such that the apoptosis induced by the
     combination of oxaliplatin and C6-ceramide is greater than the apoptosis
     induced by contacting the cancer cell with either oxaliplatin alone or
     C6-ceramide alone. This invention also provides a method of decreasing the size of a tumor, which method comprises contacting the tumor with (a)
     oxaliplatin and (b) C6-ceramide, sequentially or concomitantly, wherein
     the oxaliplatin and C6-ceramide are in amts. such that the decrease in
     tumor size induced by the combination of oxaliplatin and C6-ceramide is
     greater than the decrease in tumor size induced by contacting the tumor
     with either oxaliplatin alone or C6-ceramide alone. This invention
     further provides a pharmaceutical composition and a method for treating a
     subject afflicted with cancer.
     ANSWER 2 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN
                        2007:1087710 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         147:496093
TITLE:
                         Paclitaxel and ceramide co-administration in
                         biodegradable polymeric nanoparticulate delivery
                         system to overcome drug resistance in ovarian cancer
AUTHOR(S):
                         Devalapally, Harikrishna; Duan, Zhenfeng; Seiden,
                         Michael V.; Amiji, Mansoor M.
CORPORATE SOURCE:
                         Department of Pharmaceutical Sciences, School of
                         Pharmacy, Northeastern University, Boston, MA, USA
SOURCE:
                         International Journal of Cancer (2007), 121(8),
                         1830-1838
                         CODEN: IJCNAW; ISSN: 0020-7136
                         Wiley-Liss, Inc.
PUBLISHER:
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     The objective of this study was to overcome drug resistance upon systemic
AB
     administration of combination paclitaxel (PTX) and the apoptotic
     signaling mol. C6-ceramide (CER) in biodegradable poly(ethylene
     oxide)-modified poly(epsilon-caprolactone) (PEO-PCL) nanoparticles. S.c.
     sensitive (wild-type) and multidrug resistant (MDR-1 pos.) SKOV-3 human
     ovarian adenocarcinoma xenografts were established in female Nu/Nu mice.
     PTX and CER were administered i.v. either as a single agent or in
     combination in aqueous solution and in PEO-PCL nanoparticles to the
tumor-bearing
     mice. There was significant (p < 0.05) tumor growth suppression in both
     wild-type SKOV-3 and multidrug resistant SKOV-3TR models upon single dose
     co-administration of PTX (20 mg/kg) and CER (100 mg/kg) in nanoparticle
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formulations as compared to the individual agents and administration in aqueous solns. For instance, in SKOV-3 wild-type model, more than 4.3-fold

20071213 WO 2007-US13077

20070531

WO 2007143175

Α2

increase (p < 0.05) in tumor growth delay and 3.6-fold (p < 0.05) increase in tumor volume doubling time (DT) were observed with the combination treatment in nanoparticles as compared to untreated animals. Similarly, 3-fold increase (p < 0.05) in tumor growth delay and tumor volume DT was observed in SKOV-3TR model. Body weight changes and blood cells counts were used as measures of safety and, except for an increase in platelet counts (p < 0.05) in PTX + CER treated animals, there was no difference between various treatment strategies. The results of this study show that combination of PTX and CER in biodegradable polymeric nanoparticles can serve as a very effective therapeutic strategy to overcome drug resistance in ovarian cancer.

REFERENCE COUNT:

55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 3 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:539325 CAPLUS

DOCUMENT NUMBER: 147:157698

TITLE: Modulation of intracellular ceramide using polymeric

nanoparticles to overcome multidrug resistance in

cancer

AUTHOR(S): van Vlerken, Lilian E.; Duan, Zhenfeng; Seiden,

Michael V.; Amiji, Mansoor M.

Department of Pharmaceutical Sciences, School of CORPORATE SOURCE:

Pharmacy, Department of Hematology and Oncology,

Massachusetts General Hospital, Northeastern

University, Boston, MA, USA

SOURCE: Cancer Research (2007), 67(10), 4843-4850

CODEN: CNREA8; ISSN: 0008-5472

American Association for Cancer Research PUBLISHER:

DOCUMENT TYPE: Journal LANGUAGE: English

Although multidrug resistance (MDR) is known to develop through a variety AΒ of mol. mechanisms within the tumor cell, many tend to converge toward the alteration of apoptotic signaling. The enzyme glucosylceramide synthase (GCS), responsible for bioactivation of the proapoptotic mediator ceramide to a nonfunctional moiety glucosylceramide, is overexpressed in many MDR tumor types and has been implicated in cell survival in the presence of chemotherapy. The purpose of this study was to investigate the therapeutic strategy of coadministering ceramide with paclitaxel , a commonly used chemotherapeutic agent, in an attempt to restore apoptotic signaling and overcome MDR in the human ovarian cancer cell line SKOV3. Poly(ethylene oxide)-modified poly(epsilon-caprolactone) (PEO-PCL) nanoparticles were used to encapsulate and deliver the therapeutic agents for enhanced efficacy. Results show that indeed the cotherapy eradicates the complete population of MDR cancer cells when they are treated at their IC50 dose of paclitaxel. More interestingly, when the cotherapy was combined with the properties of nanoparticle drug delivery, the MDR cells can be resensitized to a dose of paclitaxel near the ${\tt IC50}$ of non-MDR (drug sensitive) cells, indicating a 100-fold increase in chemosensitization via this approach. Mol. anal. of activity verified the hypothesis that the efficacy of this therapeutic approach is indeed due to a restoration in apoptotic signaling, although the beneficial properties of PEO-PCL nanoparticle delivery seemed to enhance the therapeutic success even further, showing the promising potential for the clin. use of this therapeutic strategy to overcome MDR.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN T.3

ACCESSION NUMBER: 2006:1204388 CAPLUS

DOCUMENT NUMBER: 145:511655

TITLE: Nanoparticulate delivery systems comprising ceramide for treating multi-drug resistance

INVENTOR(S): Amiji, Mansoor M.; Shenoy, Dinesh B.; Vlerken, Lilian

Van

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 11pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE		DATE
PRI(US 2006257493 DRITY APPLN. INFO.:		20061116	US 2006-413067 US 2005-675837P	
AB	delivery system remulti-drug resistate treatment to a pate composition accordance amount of one or a the group consists therapeutically estimate therapeutic agents and the the co-encapsulated, adelivery to a pate localization at, a patient administ resistance reverse tamoxifen. Thus, co-encapsulated in poly (\$\varepsilon\$-caprolactor activity and cell cancer cell line acytotoxicities. It was significant en	epresentiance while tient, e. ding to the more multing of ceffective is different in a biodient in represent the ing agent (6-ceramen poly(ethe) (PCL) death we skov3 due However, whancemer	ing a qual. The simultane g., in a signer invention indrug resignation amount of a serific from the compatible, and in the multice simultaneous in the multice of cell discomposition i	in particular, a nanop different approach to cously administering the te-specific manner, is nincludes a therapeut: stance reversing agents ceramide modulators; and therapeutic agent, when he one or more multi-draw multi-drug resistance encapsulated, preferably biodegradable delivery the term of the control of the contr	overcoming c chosen drug disclosed. A ically effective s selected from a d a erein the rug resistance reversing ly vehicle for c specific eatment site in or more multi-drug fe ic ype human ovarian ual PTX and CER cells, there accns. of PTX

ANSWER 5 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:264352 CAPLUS

DOCUMENT NUMBER: 144:305123

TITLE: Combinations of ceramide and chemotherapeutic agents

for inducing tumor cell death

INVENTOR(S): Wanebo, Harold J.; Mehta, Shashikant

PATENT ASSIGNEE(S): Roger Williams Hospital, USA

SOURCE: U.S., 43 pp., Cont.-in-part of U.S. Ser. No. 287,884,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT :	NO.			KIN	D	DATE			APPL	ICAT	ION 1	NO.		D	ATE	
					_											
US 7015	251			В1		2006	0321		US 2	002-	9584	53		2	0020	424
WO 2000	0595		A1		2000	1012		WO 2	0.00 - 1	US94	40		2	0000	407	
W:	ΑE,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,
	CZ,	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,
	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,

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MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:

US 1999-287884
B2 19990407
WO 2000-US9440
W 20000407
```

This invention provides a method for increasing apoptosis in tumor cells AB and a method of decreasing a size of a tumor, said methods comprising contacting the tumor cells with: a) an effective amount of at least one antitumor chemotherapeutic agent and b) an effective amount of a ceramide, sequentially or concomitantly, wherein the apoptosis induced by the combination of the antitumor chemotherapeutic agent and the ceramide is greater than the apoptosis induced by contact of the tumor cells with either the antitumor chemotherapeutic agent alone or the ceramide alone. This invention also provides a method of treating cancer in a subject which comprises a method according to either of the above-described methods. This invention provides a method for treating cancer in a subject comprising administering to the subject an effective amount of at least one antitumor chemotherapeutic agent and an effective amount of at least one ceramide, sequentially or concomitantly. This invention provides a pharmaceutical composition comprising at least one antitumor chemotherapeutic agent in an amount effective to induce apoptosis of tumor cells and at least one ceramide in an amount effective to induce apoptosis of tumor cells and a pharmaceutically acceptable carrier.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:532671 CAPLUS

DOCUMENT NUMBER: 139:101145

TITLE: Preparation of thienopyrimidines as inhibitors of

prolylpeptidase, inducers of apoptosis and cancer

treatment agents

INVENTOR(S): Dumas, Jacques; Sibley, Robert; Wood, Jill

PATENT ASSIGNEE(S): Bayer Corporation, USA SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA.	TENT :	NO.			KIN	D	DATE			APPL	ICAT:	ION I	. OV		D.	ATE		
WO	2003	0558	90		A1	_	2003	0710		WO 2	 002-1	JS41:	 168		2	0021		
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,	
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,	
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,	
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	
		TZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW						
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,	
		KG,	KΖ,	MD,	RU,	ΤJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,	
		FΙ,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	SK,	TR,	BF,	ΒJ,	CF,	
		CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG				
AU	2002	3642	11		A1		2003	0715		AU 2	002-	3642	11		2	0021	220	
PRIORITY	Y APP	LN.	INFO	.:						US 2	001 - 1	3430	48P	I	2	0011	221	
									,	WO 2	002-1	JS41:	168	I	W 2	0021	220	
OTHER SC	TIRCE	(9) .			MARI	РΔТ	139.	1011.	45									

OTHER SOURCE(S): MARPAT 139:101145

$$\begin{array}{c|c}
R^1 & [CH_2]_q R^2 \\
\hline
S & N \\
N & X & I
\end{array}$$

1 - 4

AB The title compds. [I; X = OR3, NR3R4; R1 = H, alkyl; R2 = (un)substituted cycloalkyl, Ph, (un)saturated 4-8 membered heterocyclyl containing 1-3 heteroatoms

selected from O and S; R3 = H, alkyl; R4 = (CH2)mA, (CH2)pOA; A = (un)substituted cycloalkyl, (un)saturated 4-8 membered heterocyclyl containing

heteroatoms selected from N, O and S, etc.; or NR3R4 = (un)saturated 4-8 membered heterocyclyl containing 0-4 heteroatoms selected from N, O and S; m, p = 0-5; q = 0-1; q + (m or p) = 1-6], useful for the inhibiting the prolylpeptidase, inducing apoptosis and treating cancer, were prepared E.g., a 3-step synthesis of I [X = (2-thienylmethyl)amino; R1 = H; R2 = 4-(MeO2C)C6H4; q = 1], starting with thieno[3,2-d]pyrimidine-2,4-diol, was given. All exemplified compds. I were found to inhibit prolylpeptidase at or below of 10 $\mu \rm M$.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:532653 CAPLUS

DOCUMENT NUMBER: 139:101144

TITLE: Preparation of quinazolines and quinolines as

inhibitors of prolylpeptidase, inducers of apoptosis

and cancer treatment agents

INVENTOR(S): Dumas, Jacques; Sibley, Robert; Smith, Roger; Su,

Ning; Chen, Yuanwei; Wood, Jill; Guernon, Leatte; Dixon, Julie; Brennan, Catherine; Boyer, Stephen

PATENT ASSIGNEE(S): Bayer Corporation, USA; et al.

SOURCE: PCT Int. Appl., 266 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT 1	NO.		KIN	D	DATE		-	APPL:	ICAT	I NOI	NO.		D.	ATE	
WO 2003	 055866		A1	_	 2003	0710	•	WO 2	002-	JS41:	 176		2	0021	220
W:	AE, AG,	AL,	ΑM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
	CO, CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,
	GM, HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,
	LS, LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
	PL, PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	TZ,
	UA, UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW						
RW:	GH, GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
	KG, KZ,	MD,	RU,	ΤJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
	FI, FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	SI,	SK,	TR,	BF,	ВJ,
	CF, CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	ΤG		
AU 20023	361846		A1		2003	0715		AU 2	002-	3618	46		2	0021	220
PRIORITY APP	LN. INFO	.:						US 2	001-	3431	12P]	P 2	0011	221
							,	WO 2	002-1	JS41:	176	Ī	W 2	0021	220

OTHER SOURCE(S): MARPAT 139:101144

AB The title compds. [I or II; Z = CH, N; Y = O, S; X = OR5, NR5R6; R1, R2 = CHH, NH2, CN, halo, OH, NO2 (wherein R1 and R2 are both not H); R3 = H, alkyl; R4 = (CH2)yR41 (R41 = (un)substituted alkyl; <math>y = 0-2)], useful for the inhibiting the prolyl peptidase, inducing apoptosis and treating cancer, were prepared Thus, reacting 2,4,6-trichloroquinazoline (preparation given) with Me 4-(aminomethyl)benzoate. HCl in the presence of AcONa in H2O followed by treating the resulting Me 4-{[(2,6-dichloro-4quinazolinyl)amino]methyl}benzoate with piperidine afforded I [Z = N; X =piperidino; R1 = H; R2 = C1; R3 = H; R4 = 4-(MeO2C)C6H4CH2]. Most of the exemplified compds. I and II were found to inhibit prolylpeptidase at or below of 10 μ M.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 8 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

2003:532524 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 139:101141

TITLE: Preparation of 2,4-diaminopyrimidines as inhibitors of

prolylpeptidase, inducers of apoptosis and cancer

treatment agents

INVENTOR(S): Dumas, Jacques; Dixon, Julie; Sibley, Robert; Wood,

Jill

PATENT ASSIGNEE(S): Bayer Corporation, USA SOURCE:

PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P	'ATENT	NO.			KIN	D i	DATE			APPL	ICAT	ION I	NO.		D.	ATE	
W	0 2003	0554	 89		A1	_	2003	0710	,	 WO 2	002-	 US41	 146		2	0021:	220
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,
		LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,		
	LS, LT, LU PL, PT, RC					SC,	SD,	SE,	SG,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	TZ,
		UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW						
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	KΖ,	MD,	RU,	ΤJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	SI,	SK,	TR,	BF,	ВJ,
		CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG		
А	U 2002		A1		2003	0715		AU 2	002-	3671	72		2	0021	220		
PRIORI	TY APP	LN.	INFO	.:						US 2	001-	3430	47P]	P 2	0011	221
									,	WO 2	002-	US41	146	Ī	W 2	0021	220
OTHER	COLIDOR	/ O \			DATE TO 1		1 2 0	1 / 1 1	11								

OTHER SOURCE(S): MARPAT 139:101141

GI

$$R^{2}$$
 R^{1}
 N
 R^{4}
 R^{3}
 R^{3}

IV

$$[CH2]_{m} \stackrel{O}{=} R5$$

$$[\mathsf{CH}_2]_{\overset{\text{O}}{\mathsf{m}}} \mathsf{C} - \mathsf{R}^5$$

III

AB The title compds. [I or II; R1, R2 = H, halo, OH, etc.; R3 = H; R4 = (un)substituted alkyl, cycloalkyl, aryl, alkylaryl; or NR3R4 = (un)saturated 4-8 membered heterocyclyl which optionally contains 1-3 addnl. heteroatoms selected from N, O and S; A = III or IV; R5 = OH, OR6, NR8R9; R6 = alkyl, haloalkyl, aryl, haloaryl; R8, R9 = H, alkyl, aryl, etc.; n, m = 0-1], useful for the inhibiting prolylpeptidase, inducing apoptosis and treating cancer, were prepared E.g., a 3-step synthesis of I [A = 4-(HO2C)C6H4CH2; R1 = H; R2 = Me; R3 = H; R4 = 2-thienylmethyl], starting from Me 4-(aminomethyl)benzoate and 2,4-dichloro-5-methylpyrimidine, was given. All exemplified compds. I were found to inhibit prolylpeptidase at or below of 10 μ M.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:963204 CAPLUS

DOCUMENT NUMBER: 138:362308

TITLE: The role of MAPK pathways in the action of

chemotherapeutic drugs

AUTHOR(S): Boldt, Simone; Weidle, Ulrich H.; Kolch, Walter CORPORATE SOURCE: The Beatson Institute for Cancer Research, Cancer

Research UK, Glasgow, G61 1BD, UK

SOURCE: Carcinogenesis (2002), 23(11), 1831-1838

CODEN: CRNGDP; ISSN: 0143-3334

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal LANGUAGE: English

AB In this study we have investigated the role of mitogen-induced and stress-activated MAP kinase pathways in the cellular response to taxol, etoposide and ceramide in three different human cancer cell lines: HeLa cervical carcinoma, MCF7 breast cancer and A431 squamous carcinoma cells. The mitogen-induced ERK MAPKs were linked to cell proliferation and survival, whereas the stress-activated MAPKs, p38 and JNK, were connected with apoptosis. Our results show that all drugs activated MAPKs, but that the extent and kinetics of activation were different. In order to assay the biol. consequences of drug-induced MAPK activation we employed selective MAPK inhibitors and measured both long-term clonogenic survival as well as short-term parameters including apoptosis, mitochondrial metabolic integrity and cell cycle progression. Our results show that drug induced toxicity is not correlated with any

singular parameter, but rather a combination of effects on cell cycle and apoptosis. In certain constellations the modulation of MAPK pathways could enhance or decrease drug efficacies. These effects mainly pertained to the regulation of apoptosis and clonogenic survival, but they were highly dependent on the combination of drug and cell line without any clear patterns of correlations emerging. These results suggest that the modulation of MAPK pathways to enhance the efficacy of chemotherapeutic drugs is of limited value unless it is tailored to the specific combination of drug and cancer.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:725478 CAPLUS

DOCUMENT NUMBER: 133:276331

TITLE: Ceramide and chemotherapeutic agents for inducing cell

death in tumor cells

INVENTOR(S): Wanebo, Harold J.; Mehta, Shashikant

PATENT ASSIGNEE(S): Roger Williams Hospital, USA

SOURCE: PCT Int. Appl., 104 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

P	PATENI	NO.			KIN	D	DATE			APPL	ICAT	ION I	NO.		Dž	ATE	
W	70 200	00595	 17		A1	_	2000	1012		WO 2	000-	JS94	40		20		
	W:	ΑE,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,
		CZ,	DE,	DK,	DM,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,
		IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,
	MD, MG, M SK, SL, T					MW,	MX,	NO,	NΖ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
	SK, SL, To					TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW	
	SK, SL, TJ RW: GH, GM, KE				LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,
		DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
		CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG				
Ε	CP 120	6270			A1		2002	0522		EP 2	000-	9231	88		20	0000	407
	R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		IE,	SI,	LT,	LV,	FΙ,	RO,	MK,	CY,	AL							
U	IE, SI, LT US 7015251						2006	0321		US 2	002-	9584	53		20	0020	424
PRIORI	TY AF	PLN.	INFO	.:						US 1 WO 2				_	A2 19	9990	
										VV _	000-	J D J 4	1 0	1	rv _ \		1 0/

AB This invention provides a method for increasing apoptosis in tumor cells and a method of decreasing a size of a tumor, said methods comprising contacting the tumor cells with: (a) an effective amount of at least one antitumor chemotherapeutic agent; and (b) an effective amount of a ceramide, sequentially or concomitantly, wherein the apoptosis induced by the combination of the antitumor chemotherapeutic agent and the ceramide is greater than the apoptosis induced by contact of the tumor cells with either the antitumor chemotherapeutic agent alone or the ceramide alone. This invention also provides a method of treating cancer in a subject which comprises a method according to either of the above-described methods. This invention provides a method for treating cancer in a subject comprising administering to the subject an effective amount of at least one antitumor chemotherapeutic agent and an effective amount of at least one ceramide, sequentially or concomitantly. This invention provides a pharmaceutical composition comprising at least one antitumor chemotherapeutic agent in an amount effective to induce apoptosis of tumor cells and at least one ceramide in an amount effective to induce apoptosis of tumor cells and a pharmaceutically acceptable carrier. Paclitaxel-induced apoptosis in Jurkat cells was enhanced by

C6-N-hexanoyl-D-sphingosine.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 11 OF 15 USPATFULL on STN L3

ACCESSION NUMBER: 2007:43191 USPATFULL

TITLE: Methods and compositions for the delivery of

biologically active agents

INVENTOR(S): Esfand, Roseita, Mississauga, CANADA

Santerre, Paul J., Whitby, CANADA Yang, Meilin, Mississauga, CANADA

NUMBER KIND DATE ______ US 2007037891 A1 20070215 US 2006-404290 A1 20060414 (11) PATENT INFORMATION: APPLICATION INFO.:

> NUMBER DATE _____

PRIORITY INFORMATION: US 2005-672158P 20050415 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110, US

NUMBER OF CLAIMS: NUMBER OF DRAWINGS: 19 Drawing Page(s)
LINE COUNT: 1670
CAS INDEXTO: 48

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The invention features polymers noncovalently complexed with a biologically active agent. The polymer complexes include at least one shielding moiety covalently tethered to at least one complexing moiety,

which is complexed with at least one biologically active agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 12 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2006:301138 USPATFULL

Nanoparticulate delivery systems for treating

multi-drug resistance

Amiji, Mansoor M., Attleboro, MA, UNITED STATES INVENTOR(S):

Shenoy, Dinesh B., Boston, MA, UNITED STATES

Vlerken, Lilian van, Brookline, MA, UNITED STATES

NUMBER KIND DATE PATENT INFORMATION: US 2006257493 A1 20061116 APPLICATION INFO.: US 2006-413067 A1 20060427 (11)

> NUMBER DATE ______

US 2005-675837P 20050428 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WEINGARTEN, SCHURGIN, GAGNEBIN & LEBOVICI LLP, TEN POST

OFFICE SQUARE, BOSTON, MA, 02109, US

OFi 27 NUMBER OF CLAIMS: 1 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 3 Drawing Page(s)

741 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

An encapsulated delivery system, and, in particular, a nanoparticulate

delivery system representing a qualitatively different approach to overcoming multi-drug resistance while simultaneously administering the chosen drug treatment to a patient, e.g., in a site-specific manner, is disclosed. A composition according to the invention includes a therapeutically effective amount of one or more multi-drug resistance reversing agents selected from the group consisting of ceramide and ceramide modulators; and a therapeutically effective amount of a therapeutic agent, wherein the therapeutic agent is different from the one or more multi-drug resistance reversing agents, and the one or more multi-drug resistance reversing agents and the therapeutic agent are encapsulated, preferably co-encapsulated, in a biocompatible, biodegradable delivery vehicle for delivery to a patient in need of treatment, for example, for specific localization at, or higher probability of delivery to, a treatment site in a patient administered the composition. Preferably, the one or more multi-drug resistance reversing agents are ceramide, paclitaxel or tamoxifen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 13 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2006:70187 USPATFULL

TITLE: Combinations of ceramide and chemotherapeutic agents

for inducing tumor cell death

INVENTOR(S): Wanebo, Harold J., East Greenwich, RI, UNITED STATES

Mehta, Shashikant, Warwick, RI, UNITED STATES

PATENT ASSIGNEE(S): Roger Williams Hospital, Providence, RI, UNITED STATES

(U.S. corporation)

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 7015251	B1	20060321		
	WO 2000059517		20001012		
APPLICATION INFO.:	US 2000-958453		20000407	(9)	
	WO 2000-US9440		20000407		
			20020424	PCT 371 date	
DDIATED ADDING THE	0		C NT -	TTO 1000 207004	د نے

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1999-287884, filed

on 7 Apr 1999, ABANDONED

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Cook, Rebecca

LEGAL REPRESENTATIVE: White, Esq., John P., Cooper & Dunham LLP

NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 47 Drawing Figure(s); 24 Drawing Page(s)

LINE COUNT: 2051

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a method for increasing apoptosis in tumor cells AΒ and a method of decreasing a size of a tumor, said methods comprising contacting the tumor cells with: a) an effective amount of at least one antitumor chemotherapeutic agent and b) an effective amount of a ceramide, sequentially or concomitantly, wherein the apoptosis induced by the combination of the antitumor chemotherapeutic agent and the ceramide is greater than the apoptosis induced by contact of the tumor cells with either the antitumor chemotherapeutic agent alone or the ceramide alone. This invention also provides a method of treating cancer in a subject which comprises a method according to either of the above-described methods. This invention provides a method for treating cancer in a subject comprising administering to the subject an effective amount of at least one antitumor chemotherapeutic agent and an effective amount of at least one ceramide, sequentially or concomitantly. This invention provides a pharmaceutical composition comprising at least one antitumor chemotherapeutic agent in an amount effective to induce

apoptosis of tumor cells and at least one ceramide in an amount effective to induce apoptosis of tumor cells and a pharmaceutically acceptable carrier.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 14 OF 15 USPATFULL on STN

ACCESSION NUMBER: 2005:30390 USPATFULL

TITLE: Method and system for systemic delivery of growth

> arresting, lipid-derived bioactive compounds Kester, Mark, Harrisburg, PA, UNITED STATES Stover, Thomas, Hershey, PA, UNITED STATES

Lowe, Tao, Hershey, PA, UNITED STATES

Adair, James, UNITED STATES

Kim, Young Shin, Hershey, PA, UNITED STATES

KIND DATE NUMBER _____ US 2005025820 A1 20050203 US 2004-835520 A1 20040426 (10) PATENT INFORMATION: APPLICATION INFO.:

NUMBER DATE _____ PRIORITY INFORMATION:

US 2003-465938P 20030425 (60) US 2003-465937P 20030428 (60)

DOCUMENT TYPE: Utility APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: Barbara E. Johnson, WEBB ZIESENHEIM LOGSDON ORKIN &

HANSON, P.C., 700 Koppers Building, 436 Seventh Avenue,

Pittsburgh, PA, 15219-1818

77 NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1

INVENTOR(S):

NUMBER OF DRAWINGS: 20 Drawing Page(s)

LINE COUNT: 1954

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A system and method for optimizing the systemic delivery of growth-arresting lipid-derived bioactive drugs or gene therapy agents to an animal or human in need of such agents utilizing nanoscale assembly systems, such as liposomes, resorbable and non-aggregating nanoparticle dispersions, metal or semiconductor nanoparticles, or polymeric materials such as dendrimers or hydrogels, each of which exhibit improved lipid solubility, cell permeability, an increased circulation half life and pharmacokinetic profile with improved tumor or vascular targeting.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 15 OF 15 USPATFULL on STN

2004:285842 USPATFULL ACCESSION NUMBER:

Drug formulations for coating medical devices TITLE: INVENTOR(S): Schultz, Robert K., Poway, CA, UNITED STATES

NUMBER KIND DATE US 2004224003 A1 20041111 US 2004-773756 A1 20040206 (10) PATENT INFORMATION: APPLICATION INFO.:

NUMBER DATE

PRIORITY INFORMATION: US 2003-446318P 20030207 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICAT APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: KNOBBE MARTENS OLSON & BEAR LLP, 2040 MAIN STREET,

FOURTEENTH FLOOR, IRVINE, CA, 92614

NUMBER OF CLAIMS: 22 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 1 Drawing Page(s)

LINE COUNT: 361

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to oil-based formulations of hydrophobic drugs for the uniform coating of medical devices such as vascular stents

and balloons. Another aspect of the present invention is an

intravascular medical device having an oil-based coating suitable for

delivering a water-insoluble drug, comprising one or more of an anti-oxidant, an anti-inflammatory and an anti-restenotic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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(FILE 'HOME' ENTERED AT 10:16:05 ON 12 FEB 2008)

FILE 'REGISTRY' ENTERED AT 10:16:44 ON 12 FEB 2008 E "N-HEXANOYL-D-SPHINGOSINE"/CN 25

L1 1 S E1

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:18:02 ON 12 FEB

L2 240 S L1

L3 15 S L2 AND (PACLITAXEL OR TAXOL)

=> s 12 and (?cancer? or ?tumor?)

L4 78 L2 AND (?CANCER? OR ?TUMOR?)

=> s 14 and combination?

L5 22 L4 AND COMBINATION?

=> d 15 1-22 ibib, abs

L5 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1420210 CAPLUS

DOCUMENT NUMBER: 148:24415

TITLE: ceramide and oxaliplatin combination for

cancer therapy

INVENTOR(S): Wanebo, Harold J.

PATENT ASSIGNEE(S): Roger Williams Hospital, USA

SOURCE: PCT Int. Appl., 50pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PAI	ENT	NO.			KIN	D i	DATE			APPL	ICAT	ION 1	NO.		D.	ATE	
	2007				A2 A3		 2007: 2008:		,	WO 2	007-	US13	077		2	0070	531
WO	O 2007143175 W: AE, AG, A: CH, CN, CO			•	AM,	AT,	AU,	AZ,	•	•	•	•	•	•	•	•	•
		GB,	GD,	GE,	GH,	GM,	GT,	HN,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,
	GB, GD, GE KM, KN, KE MG, MK, MN		•	•	•	•	•	•	•	•	•	•	•	•			
		PT,	RO,	RS,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SM,	SV,	SY,	ΤJ,	TM,	TN,

TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA US 2008033039 A1 20080207 US 2007-809418 20070531 PRIORITY APPLN. INFO.: US 2006-810243P P 20060602 This invention provides a method for increasing apoptosis in a cancer cell comprising contacting the cancer cell with (a) oxaliplatin and (b) C6-ceramide, sequentially or concomitantly, wherein the oxaliplatin and C6-ceramide are in amts. such that the apoptosis induced by the combination of oxaliplatin and C6-ceramide is greater than the apoptosis induced by contacting the cancer cell with either oxaliplatin alone or C6-ceramide alone. This invention also provides a method of decreasing the size of a tumor, which method comprises contacting the tumor with (a) oxaliplatin and (b) C6-ceramide, sequentially or concomitantly, wherein the oxaliplatin and C6-ceramide are in amts. such that the decrease in tumor size induced by the combination of oxaliplatin and C6-ceramide is greater than the decrease in tumor size induced by contacting the tumor with either oxaliplatin alone or C6-ceramide alone. This invention further provides a pharmaceutical composition and a method for treating a subject afflicted with cancer.

L5 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1087710 CAPLUS

DOCUMENT NUMBER: 147:496093

TITLE: Paclitaxel and ceramide co-administration in biodegradable polymeric nanoparticulate delivery

system to overcome drug resistance in ovarian

cancer

AUTHOR(S): Devalapally, Harikrishna; Duan, Zhenfeng; Seiden,

Michael V.; Amiji, Mansoor M.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of

Pharmacy, Northeastern University, Boston, MA, USA

SOURCE: International Journal of Cancer (2007), 121(8),

1830-1838

CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

AB The objective of this study was to overcome drug resistance upon systemic administration of combination paclitaxel (PTX) and the apoptotic signaling mol. C6-ceramide (CER) in biodegradable poly(ethylene oxide)-modified poly(epsilon-caprolactone) (PEO-PCL) nanoparticles. S.c. sensitive (wild-type) and multidrug resistant (MDR-1 pos.) SKOV-3 human ovarian adenocarcinoma xenografts were established in female Nu/Nu mice. PTX and CER were administered i.v. either as a single agent or in combination in aqueous solution and in PEO-PCL nanoparticles to the tumor-bearing mice. There was significant (p < 0.05)tumor growth suppression in both wild-type SKOV-3 and multidrug resistant SKOV-3TR models upon single dose co-administration of PTX (20 mg/kg) and CER (100 mg/kg) in nanoparticle formulations as compared to the individual agents and administration in aqueous solns. For instance, in SKOV-3 wild-type model, more than 4.3-fold increase (p < 0.05) in tumor growth delay and 3.6-fold (p < 0.05) increase in tumor volume doubling time (DT) were observed with the combination treatment in nanoparticles as compared to untreated animals. Similarly, 3-fold increase (p < 0.05) in tumor growth delay and tumor volume DT was observed in SKOV-3TR model. Body weight

changes and blood cells counts were used as measures of safety and, except for an increase in platelet counts (p < 0.05) in PTX + CER treated animals, there was no difference between various treatment strategies. The results of this study show that combination of PTX and CER in biodegradable polymeric nanoparticles can serve as a very effective therapeutic strategy to overcome drug resistance in ovarian cancer

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1030640 CAPLUS

DOCUMENT NUMBER: 147:335807

TITLE: Role of Acid Ceramidase in Resistance to FasL: Therapeutic Approaches Based on Acid Ceramidase

Inhibitors and FasL Gene Therapy

AUTHOR(S): Elojeimy, Saeed; Liu, Xiang; Mckillop, John C.;

El-Zawahry, Ahmed M.; Holman, David H.; Cheng,

Jonathan Y.; Meacham, William D.; Mahdy, Ayman E. M.; Saad, Antonio F.; Turner, Lorianne S.; Cheng, Joseph; Day, Terrence A.; Dong, Jian-Yun; Bielawska, Alicja;

Hannun, Yusuf A.; Norris, James Scott

CORPORATE SOURCE: Department of Microbiology and Immunology, Medical

University of South Carolina, Charleston, SC, USA

SOURCE: Molecular Therapy (2007), 15(7), 1259-1263

CODEN: MTOHCK; ISSN: 1525-0016

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal LANGUAGE: English

Head and neck squamous cell cancers (HNSCC) are particularly aggressive and are resistant to many forms of treatment. Ceramide metabolism has been shown to play an important role in cancer progression and cancer resistance to therapy in many tumor models, including HNSCC. Here, we study the role of the ceramide-metabolizing enzyme acid ceramidase (AC) in therapeutic responses in HNSCC. First, we show that AC is over-expressed in 70% of head and neck squamous cell tumors compared with normal tissues, suggesting that this enzyme may play an important role in facilitating HNSCC growth. Next, comparison of three HNSCC cell lines with low, medium, and high levels of AC reveals an inverse correlation between the levels of AC and their response to exogenous C-6-ceramide. Furthermore, over-expression of AC in SCC-1 cells increased resistance to Fas-induced cell killing. Conversely, down-regulation of AC using specific AC small interfering RNA (siRNA) sensitized the SCC-1 cancer cell line to Fas-induced apoptosis. Finally, we show that the AC inhibitor LCL 204 can sensitize HNSCC cell lines to Fas-induced apoptosis both in vitro and in a xenograft model in vivo, suggesting that the combination of FasL gene therapy and LCL 204 may become a new treatment option for advanced-stage head and neck cancer.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:539325 CAPLUS

DOCUMENT NUMBER: 147:157698

TITLE: Modulation of intracellular ceramide using polymeric

nanoparticles to overcome multidrug resistance in

cancer

AUTHOR(S): van Vlerken, Lilian E.; Duan, Zhenfeng; Seiden,

Michael V.; Amiji, Mansoor M.

CORPORATE SOURCE: Department of Pharmaceutical Sciences, School of

Pharmacy, Department of Hematology and Oncology,

Massachusetts General Hospital, Northeastern

University, Boston, MA, USA

SOURCE: Cancer Research (2007), 67(10), 4843-4850

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal LANGUAGE: English

Although multidrug resistance (MDR) is known to develop through a variety AB of mol. mechanisms within the tumor cell, many tend to converge toward the alteration of apoptotic signaling. The enzyme glucosylceramide synthase (GCS), responsible for bioactivation of the proapoptotic mediator ceramide to a nonfunctional moiety glucosylceramide, is overexpressed in many MDR tumor types and has been implicated in cell survival in the presence of chemotherapy. The purpose of this study was to investigate the therapeutic strategy of coadministering ceramide with paclitaxel, a commonly used chemotherapeutic agent, in an attempt to restore apoptotic signaling and overcome MDR in the human ovarian cancer cell line SKOV3. Poly(ethylene oxide)-modified poly(epsilon-caprolactone) (PEO-PCL) nanoparticles were used to encapsulate and deliver the therapeutic agents for enhanced efficacy. Results show that indeed the cotherapy eradicates the complete population of MDR cancer cells when they are treated at their IC50 dose of paclitaxel. More interestingly, when the cotherapy was combined with the properties of nanoparticle drug delivery, the MDR cells can be resensitized to a dose of paclitaxel near the IC50 of non-MDR (drug sensitive) cells, indicating a 100-fold increase in chemosensitization via this approach. Mol. anal. of activity verified the hypothesis that the efficacy of this therapeutic approach is indeed due to a restoration in apoptotic signaling, although the beneficial properties of PEO-PCL nanoparticle delivery seemed to enhance the therapeutic success even further, showing the promising potential for the clin. use of this therapeutic strategy to overcome MDR.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1204388 CAPLUS

DOCUMENT NUMBER: 145:511655

TITLE: Nanoparticulate delivery systems comprising ceramide

for treating multi-drug resistance

INVENTOR(S): Amiji, Mansoor M.; Shenoy, Dinesh B.; Vlerken, Lilian

Van

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 11pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2006257493	A1	20061116	US 2006-413067	20060427
	RITY APPLN. INFO.:				P 20050428
AB	An encapsulated del	ivery s	ystem, and,	in particular, a nano	particulate
				ifferent approach to	
	multi-drug resistar	ice whil	e simultaneo	usly administering th	e chosen drug
				e-specific manner, is	
	composition accordi	ng to t	he invention	includes a therapeut	ically effecti

the group consisting of ceramide and ceramide modulators; and a therapeutically effective amount of a therapeutic agent, wherein the

amount of one or more multi-drug resistance reversing agents selected from

therapeutic agent is different from the one or more multi-drug resistance reversing agents, and the one or more multi-drug resistance reversing agents and the therapeutic agent are encapsulated, preferably co-encapsulated, in a biocompatible, biodegradable delivery vehicle for delivery to a patient in need of treatment, for example, for specific localization at, or higher probability of delivery to, a treatment site in a patient administered the composition Preferably, the one or more multi-drug resistance reversing agents are ceramide, paclitaxel or tamoxifen. Thus, C6-ceramide (CER) and paclitaxel (PAX) were co-encapsulated in poly(ethylene oxide) (PEO)-modified poly(ε -caprolactone) (PCL) nanoparticles. Enhanced apoptotic activity and cell death were observed in vitro in the wildtype human ovarian cancer cell line SKOV3 due to an additive effect of individual PTX and CER cytotoxicities. However, in the multi-drug resistant (MDR) cells, there was significant enhancement of cell death when combining concns. of PTX and CER that individually did not result in significant cell killing.

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

2006:469652 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 144:474951

TITLE: A composition comprising a stable lipid assembly for

combination therapy of proliferative disorders

Barenholz, Yechezkel; Khazanov, Elena INVENTOR(S):

PATENT ASSIGNEE(S): University of Jerusalem Yissum Research Development

Company of the Hebrew, Israel

PCT Int. Appl., 56 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PA:	TENT	ΝΟ.			KIN		DATE			APPL	ICAT	ION I	ΝΟ.		D.	ATE	
	2006 2006				A2		2006 2006		,	WO 2	005-	IL12	00		2	0051	115
	W:	CN, GE, KZ, MZ, SG,	CO, GH, LC, NA, SK,	CR, GM, LK, NG, SL,	CU, HR, LR, NI, SM,	CZ, HU, LS, NO, SY,	AU, DE, ID, LT, NZ, TJ,	DK, IL, LU, OM,	DM, IN, LV, PG,	DZ, IS, LY, PH,	EC, JP, MA, PL,	EE, KE, MD, PT,	EG, KG, MG, RO,	ES, KM, MK, RU,	FI, KN, MN, SC,	GB, KP, MW, SD,	GD, KR, MX, SE,
	SG, SK, SL, VN, YU, ZA, VN, YU, ZA, RW: AT, BE, BG, IS, IT, LT, CF, CG, CI, GM, KE, LS, KG, KZ, MD,					CY, LV, GA, MZ,	MC, GN, NA,	NL, GQ,	PL, GW,	PT, ML,	RO, MR,	SE, NE,	SI, SN,	SK, TD,	TR, TG,	BF, BW,	BJ, GH,
	2005																
EP CN	1011	004 AT, IS, 0275	BE, IT, 2	BG, LI,	A2 CH, LT, A	CY, LU,	2007 CZ, LV, 2008	0815 DE, MC, 0109	DK, NL,	EP 2 EE, PL, CN 2	005- ES, PT, 005-	8037 FI, RO, 8004	47 FR, SE, 5520	GB, SI,	2 GR, SK, 2	0051 HU, TR 0051	115 IE, 115
IN PRIORIT	2007 Y APP						2007		,	US 2	004-	6272	74 81P 00		P 2	0070 0041 0051	115

OTHER SOURCE(S): MARPAT 144:474951

The present invention concerns a new medical treatment involving the combination of two active entities, as well as pharmaceutical compns. comprising the two active entities. Specifically, the invention provides a pharmaceutical composition comprising a stable lipid assembly

comprising as a first active entity an apoptosis-affecting lipid which does not self-aggregate in a polar environment to form liposomes and a lipopolymer. The pharmaceutical composition further comprises, as the second active entity, a cytotoxic amphipathic weak base drug carried by the lipid assembly or by a different liposome. According to one embodiment, the apoptosis-affecting lipid is a pro-apoptotic lipid. A preferred pro-apoptotic lipid is ceramide, preferably C6-ceramide. The cytotoxic amphipathic weak base drug is preferably doxorubicin or a biol. active, anthracycline-based doxorubicin analog thereof. Thus, doxorubicin was incorporated into sterically stabilized liposomes (SSL) composed of hydrogenated soybean phosphatidylcholine (HSPC) or DSPC liposome-forming lipid, stabilized by lipopolymer N-carbamyl-poly(ethylene glycol Me ether)-1,2-distearoyl-sn-glycero-3-phosphoethanolamine tri-Et ammonium salt (2kPEG-DSPE, 7.5 mol%), and having either 11.5 or 23 mol% of C6-Cer. The liposomes accumulated in tumor at much higher level than free doxorubicin, explaining superior therapeutic activity and reduced systemic and cardiac toxicity of doxorubicin delivered via SSL compared with free doxorubicin.

L5 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:456192 CAPLUS

DOCUMENT NUMBER: 145:327844

TITLE: Lactoferricin-induced apoptosis in

estrogen-nonresponsive MDA-MB-435 breast cancer cells is enhanced by C6 ceramide or

tamoxifen

AUTHOR(S): Furlong, Suzanne J.; Mader, Jamie S.; Hoskin, David W.

CORPORATE SOURCE: Department of Microbiology and Immunology, Faculty of

Medicine, Dalhousie University, Halifax, NS, B3H 1X5,

Can.

SOURCE: Oncology Reports (2006), 15(5), 1385-1390

CODEN: OCRPEW; ISSN: 1021-335X

PUBLISHER: Oncology Reports

DOCUMENT TYPE: Journal LANGUAGE: English

AB Bovine lactoferricin (LfcinB) is a cationic peptide that selectively induces caspase-dependent apoptosis in human leukemia and carcinoma cell lines. Ceramide is a second messenger in apoptosis signaling that has been shown to increase the cytotoxicity of various anti-cancer drugs. In this study, we determined whether manipulation of intracellular ceramide levels enhanced LfcinB-induced apoptosis of estrogennonresponsive MDA-MB-435 breast carcinoma cells. LfcinB caused DNA fragmentation and morphol. changes consistent with apoptosis in MDA-MB-435 breast cancer cell cultures, but did not affect the viability of untransformed mammary epithelial cells. MDA-MB-435 breast cancer cells also exhibited DNA fragmentation and morphol. changes consistent with apoptosis following exposure to the cell-permeable ceramide analog C6. An additive increase in DNA fragmentation was observed when both LfcinB and C6 ceramide were added to MDA-MB-435 breast cancer cell cultures. A greater than additive increase in DNA fragmentation was seen when LfcinB was used in combination with tamoxifen, which prevents the metabolism of endogenous ceramide to glucosylceramide by glucosylceramide synthase, as well as blocking estrogen receptor signaling. However, a selective inhibitor of glucosyl-ceramide synthase, 1-phenyl-2-palmitoylamino-3-morpholino-1-propanol, failed to further increase DNA fragmentation by LfcinB, suggesting that tamoxifen enhanced LfcinB-induced apoptosis in breast cancer cells via a mechanism that did not involve glucosylceramide synthase inhibition. We conclude that combination therapy with LfcinB and tamoxifen warrants further investigation for possible use in the treatment of breast cancer.

L5 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:264352 CAPLUS

DOCUMENT NUMBER: 144:305123

TITLE: Combinations of ceramide and

chemotherapeutic agents for inducing tumor

cell death

INVENTOR(S): Wanebo, Harold J.; Mehta, Shashikant

PATENT ASSIGNEE(S): Roger Williams Hospital, USA

SOURCE: U.S., 43 pp., Cont.-in-part of U.S. Ser. No. 287,884,

abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

1	PAI	ENT 1	NO.			KIN	D	DATE			APPL	ICAT	ION I	NO.		D.	ATE	
		7015				B1		2006			 US 2					_	0020	
Ī	WO	2000	0595	17		A1		2000	1012		WO 2	000-1	US94	40		2	0000	407
		W:	ΑE,	AL,	ΑM,	ΑT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,
			CZ,	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,
		CZ, DE, DK, IN, IS, JP,				KE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,
			MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
			SK,	SL,	ΤJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW	
		RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,
			DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
			CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG						
PRIOR	ITY	APP:	LN.	INFO	.:						US 1	999-	2878	84		B2 1	9990	407
											WO 2	000-1	US94	40	,	W 2	0000	407

This invention provides a method for increasing apoptosis in tumor AB cells and a method of decreasing a size of a tumor, said methods comprising contacting the tumor cells with: a) an effective amount of at least one antitumor chemotherapeutic agent and b) an effective amount of a ceramide, sequentially or concomitantly, wherein the apoptosis induced by the combination of the antitumor chemotherapeutic agent and the ceramide is greater than the apoptosis induced by contact of the tumor cells with either the antitumor chemotherapeutic agent alone or the ceramide alone. This invention also provides a method of treating cancer in a subject which comprises a method according to either of the above-described methods. This invention provides a method for treating cancer in a subject comprising administering to the subject an effective amount of at least one antitumor chemotherapeutic agent and an effective amount of at least one ceramide, sequentially or concomitantly. This invention provides a pharmaceutical composition comprising at least one antitumor chemotherapeutic agent in an amount effective to induce apoptosis of tumor cells and at least one ceramide in an amount effective to induce apoptosis of tumor cells and a pharmaceutically acceptable carrier.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:129173 CAPLUS

DOCUMENT NUMBER: 141:235794

TITLE: N-hexanoyl-sphingomyelin potentiates in vitro doxorubicin cytotoxicity by enhancing its cellular

influx

AUTHOR(S): Veldman, R. J.; Zerp, S.; van Blitterswijk, W. J.;

Verheij, M.

CORPORATE SOURCE: The Netherlands Cancer Institute, Division of Cellular

Biochemistry, Antoni van Leeuwenhoek Hospital,

Amsterdam, NL-1066 CX, Neth.

SOURCE: British Journal of Cancer (2004), 90(4), 917-925

CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal LANGUAGE: English

AB Anticancer drugs generally have intracellular targets,

implicating transport over the plasma membrane. For amphiphilic agents, such as the anthracycline doxorubicin, this occurs by passive diffusion. We investigated whether exogenous membrane-permeable lipid analogs improve this drug influx. Combinations of drugs and lipid analogs were coadministered to cultured endothelial cells and various tumor cell lines, and subsequent drug accumulation in cells was quantified. identified N-hexanoyl-sphingomyelin (SM) as a potent enhancer of drug uptake. Low micromolar amts. of this short-chain sphingolipid, being not toxic itself, enhanced the uptake of doxorubicin up to 300% and decreased its EC50 toxicity values seven- to 14-fold. N-hexanoyl SM acts at the level of the plasma membrane, but was found not incorporated in (isolated) lipid rafts, and artificial disruption or elimination of raft constituents did not affect its drug uptake-enhancing effect. Further, any mechanistic role of the endocytic machinery, membrane leakage or ABC-transportermediated efflux could be excluded. Finally, a correlation was established between the degree of drug lipophilicity, as defined by partitioning in a two-phase octanol-water system, and the susceptibility of the drug towards the uptake-enhancing effect of the sphingolipid. A clear optimum was found for amphiphilic drugs, such as doxorubicin, epirubicin and topotecan, indicating that N-hexanoyl-SM might act by modulating the average degree of plasma membrane lipophilicity, in turn facilitating transbilayer drug diffusion. The concept of short-chain sphingolipids as amphiphilic drug potentiators provides novel opportunities for improving drug delivery technologies.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:532671 CAPLUS

DOCUMENT NUMBER: 139:101145

TITLE: Preparation of thienopyrimidines as inhibitors of

prolylpeptidase, inducers of apoptosis and

cancer treatment agents

INVENTOR(S): Dumas, Jacques; Sibley, Robert; Wood, Jill

PATENT ASSIGNEE(S): Bayer Corporation, USA SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PAI	ENT :	NO.			KIN	D	DATE			APPL	ICAT	ION :	NO.		D	ATE	
						_									_		
WO	2003	05589	90		A1		2003	0710	,	WO 2	002-	US41	168		2	0021	220
	W:	···,,		AL,	ΑM,	ΑT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO, CR, CU		CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SI,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,
	PL, PT, RC TZ, UA, UG		UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW						
	RW:	GH,	GM,	KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,

KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,

CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002364211 A1 20030715 AU 2002-364211 20021220 PRIORITY APPLN. INFO.: US 2001-343048P P 20011221 WO 2002-US41168 W 20021220

OTHER SOURCE(S): MARPAT 139:101145

GΙ

$$\begin{array}{c|c}
R^1 & [CH_2]_{\overline{q}} R^2 \\
S & N \\
N & X
\end{array}$$

AB The title compds. [I; X = OR3, NR3R4; R1 = H, alkyl; R2 = (un)substituted cycloalkyl, Ph, (un)saturated 4-8 membered heterocyclyl containing 1-3 heteroatoms

selected from O and S; R3 = H, alkyl; R4 = (CH2)mA, (CH2)pOA; A = $(un)substituted\ cycloalkyl$, $(un)saturated\ 4-8\ membered\ heterocyclyl\ containing$ 1-4

heteroatoms selected from N, O and S, etc.; or NR3R4 = (un)saturated 4-8 membered heterocyclyl containing 0-4 heteroatoms selected from N, O and S; m, p = 0-5; q = 0-1; q + (m or p) = 1-6], useful for the inhibiting the prolylpeptidase, inducing apoptosis and treating cancer, were prepared E.g., a 3-step synthesis of I [X = (2-thienylmethyl)amino; R1 = H; R2 = 4-(MeO2C)C6H4; q = 1], starting with thieno[3,2-d]pyrimidine-2,4-diol, was given. All exemplified compds. I were found to inhibit prolylpeptidase at or below of 10 μ M.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:532653 CAPLUS

DOCUMENT NUMBER: 139:101144

TITLE: Preparation of quinazolines and quinolines as

inhibitors of prolylpeptidase, inducers of apoptosis

and cancer treatment agents

INVENTOR(S): Dumas, Jacques; Sibley, Robert; Smith, Roger; Su,

Ning; Chen, Yuanwei; Wood, Jill; Guernon, Leatte; Dixon, Julie; Brennan, Catherine; Boyer, Stephen

PATENT ASSIGNEE(S): Bayer Corporation, USA; et al.

SOURCE: PCT Int. Appl., 266 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.				KIND		DATE			APPLICATION NO.				DATE				
						-									_		
WO	2003	0558	66		A1 20030710			1	WO 2002-US41176				20021220				
	W:	ΑE,	AG,	AL,	ΑM,	AT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	TZ,

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,

CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002361846 A1 20030715 AU 2002-361846 20021220 PRIORITY APPLN. INFO.: US 2001-343112P P 20011221

WO 2002-US41176 W 20021220

OTHER SOURCE(S): MARPAT 139:101144

GΙ

$$R^2$$
 R^1
 R^4
 R^4

AB The title compds. [I or II; Z = CH, N; Y = O, S; X = OR5, NR5R6; R1, R2 = H, NH2, CN, halo, OH, NO2 (wherein R1 and R2 are both not H); R3 = H, alkyl; R4 = (CH2)yR41 (R41 = (un)substituted alkyl; y = 0-2)], useful for the inhibiting the prolyl peptidase, inducing apoptosis and treating cancer, were prepared Thus, reacting 2,4,6-trichloroquinazoline (preparation given) with Me 4-(aminomethyl)benzoate.HCl in the presence of AcONa in H2O followed by treating the resulting Me 4-{[(2,6-dichloro-4-quinazolinyl)amino]methyl}benzoate with piperidine afforded I [Z = N; X = piperidino; R1 = H; R2 = C1; R3 = H; R4 = 4-(MeO2C)C6H4CH2]. Most of the exemplified compds. I and II were found to inhibit prolylpeptidase at or below of 10 μ M.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:532524 CAPLUS

DOCUMENT NUMBER: 139:101141

TITLE: Preparation of 2,4-diaminopyrimidines as inhibitors of

prolylpeptidase, inducers of apoptosis and

cancer treatment agents

INVENTOR(S): Dumas, Jacques; Dixon, Julie; Sibley, Robert; Wood,

Jill

PATENT ASSIGNEE(S): Bayer Corporation, USA SOURCE: PCT Int. Appl., 47 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT NO.				KIN	D :	DATE			APPL	ICAT	ION I	. O <i>V</i>		D	ATE		
						_											
WO	2003	0554	89		A1 20030710			1	WO 2002-US41146				20021220				
	W:	ΑE,	AG,	AL,	ΑM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NΖ,	OM,	PH,
		PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	ΤJ,	TM,	TN,	TR,	TT,	${\sf TZ}$,

UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002367172 20030715 AU 2002-367172 Α1 20021220 PRIORITY APPLN. INFO.: US 2001-343047P Ρ 20011221 WO 2002-US41146 W 20021220

OTHER SOURCE(S): MARPAT 139:101141

$$[CH_2]_{\overline{m}} \stackrel{O}{=} R5$$

$$[CH_2]_{\overline{m}} \stackrel{O}{=} R5$$

$$[III]$$

$$IV$$

AΒ The title compds. [I or II; R1, R2 = H, halo, OH, etc.; R3 = H; R4 = (un) substituted alkyl, cycloalkyl, aryl, alkylaryl; or NR3R4 = (un) saturated 4-8 membered heterocyclyl which optionally contains 1-3 addnl. heteroatoms selected from N, O and S; A = III or IV; R5 = OH, OR6, NR8R9; R6 = alkyl, haloalkyl, aryl, haloaryl; R8, R9 = H, alkyl, aryl, etc.; n, m = 0-1], useful for the inhibiting prolylpeptidase, inducing apoptosis and treating cancer, were prepared E.g., a 3-step synthesis of I [A =4-(HO2C)C6H4CH2; R1 = H; R2 = Me; R3 = H; R4 = 2-thienylmethyl], starting from Me 4-(aminomethyl)benzoate and 2,4-dichloro-5-methylpyrimidine, was given. All exemplified compds. I were found to inhibit prolylpeptidase at or below of 10 μM .

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 13 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

2002:963204 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 138:362308

TITLE: The role of MAPK pathways in the action of

chemotherapeutic drugs

Boldt, Simone; Weidle, Ulrich H.; Kolch, Walter AUTHOR(S): The Beatson Institute for Cancer Research, Cancer CORPORATE SOURCE:

Research UK, Glasgow, G61 1BD, UK

SOURCE: Carcinogenesis (2002), 23(11), 1831-1838

CODEN: CRNGDP; ISSN: 0143-3334

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal LANGUAGE: English

In this study we have investigated the role of mitogen-induced and AΒ stress-activated MAP kinase pathways in the cellular response to taxol, etoposide and ceramide in three different human cancer cell lines: HeLa cervical carcinoma, MCF7 breast cancer and A431 squamous carcinoma cells. The mitogen-induced ERK MAPKs were linked to cell proliferation and survival, whereas the stress-activated MAPKs, p38 and JNK, were connected with apoptosis. Our results show that all drugs activated MAPKs, but that the extent and kinetics of activation were different. In order to assay the biol. consequences of drug-induced MAPK activation we employed selective MAPK inhibitors and measured both long-term clonogenic survival as well as short-term parameters including apoptosis, mitochondrial metabolic integrity and cell cycle progression. Our results show that drug induced toxicity is not correlated with any singular parameter, but rather a combination of effects on cell cycle and apoptosis. In certain constellations the modulation of MAPK pathways could enhance or decrease drug efficacies. These effects mainly pertained to the regulation of apoptosis and clonogenic survival, but they were highly dependent on the combination of drug and cell line without any clear patterns of correlations emerging. These results suggest that the modulation of MAPK pathways to enhance the efficacy of chemotherapeutic drugs is of limited value unless it is tailored to the specific combination of drug and cancer.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:725478 CAPLUS

DOCUMENT NUMBER: 133:276331

TITLE: Ceramide and chemotherapeutic agents for inducing cell

death in tumor cells

INVENTOR(S): Wanebo, Harold J.; Mehta, Shashikant

PATENT ASSIGNEE(S): Roger Williams Hospital, USA

SOURCE: PCT Int. Appl., 104 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

	PATENT NO.				KIND DATE			APPLICATION NO.				DATE						
	WO	2000	0595	 17		A1 20001012			WO 2000-US9440				20000407					
		W:	ΑE,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,
			CZ,	DE,	DK,	DM,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,
			IN,	IS,	JP,	KE,	KG,	KP,	KR,	KΖ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MA,
			MD,	MG,	MK,	MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
			SK,	SL,	ΤJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UΖ,	VN,	YU,	ZA,	ZW	
		RW:	GH,	GM,	KΕ,	LS,	MW,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	DE,
			DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,
			CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	ΤG				
	ΕP	1206	270			A1		2002	0522	EP 2000-923188					20000407			
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	MC,	PT,
			IE,	SI,	LT,	LV,	FI,	RO,	MK,	CY,	AL							
	US	7015	251			В1		2006	0321		US 2	002-	9584	53		2	0020	424
PRIOF	IORITY APPLN. INFO.:								US 1999-287884			i	A2 19990407					
											WO 2	000-	US94	40	Ī	W 2	0000	407

AB This invention provides a method for increasing apoptosis in tumor cells and a method of decreasing a size of a tumor, said methods comprising contacting the tumor cells with: (a) an effective amount of at least one antitumor chemotherapeutic agent; and (b) an effective amount of a ceramide, sequentially or concomitantly, wherein the apoptosis induced by the combination of the

antitumor chemotherapeutic agent and the ceramide is greater than the apoptosis induced by contact of the tumor cells with either the antitumor chemotherapeutic agent alone or the ceramide alone. This invention also provides a method of treating cancer in a subject which comprises a method according to either of the above-described methods. This invention provides a method for treating cancer in a subject comprising administering to the subject an effective amount of at least one antitumor chemotherapeutic agent and an effective amount of at least one ceramide, sequentially or concomitantly. This invention provides a pharmaceutical composition comprising at least one antitumor chemotherapeutic agent in an amount effective to induce apoptosis of tumor cells and at least one ceramide in an amount effective to induce apoptosis of tumor cells and a pharmaceutically acceptable carrier. Paclitaxel-induced apoptosis in Jurkat cells was enhanced by C6-N-hexanoyl-D-sphingosine.

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 1

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2007:127957 USPATFULL

SYSTEMS AND METHODS FOR SELECTION AND MAINTENANCE OF TITLE:

HOMOGENEOUS AND PLURIPOTENT HUMAN EMBRYONIC CELLS

Salli, Ugar, Hummelstown, PA, UNITED STATES INVENTOR(S):

Kester, Mark, Harrisburg, PA, UNITED STATES Vrana, Kent E., Hummelstown, PA, UNITED STATES

The Penn State Research Foundation (U.S. corporation) PATENT ASSIGNEE(S):

> NUMBER KIND DATE ______

PATENT INFORMATION: US 2007111306 A1 20070517 US 2006-557791 A1 20061108 (11)

APPLICATION INFO.:

NUMBER DATE _____

US 2005-734862P 20051109 (60) PRIORITY INFORMATION:

Utility DOCUMENT TYPE: FILE SEGMENT: APPLICATION

BOX 7021, TROY, MI, 48007-7021, US 30 LEGAL REPRESENTATIVE: GIFFORD, KRASS, SPRINKLE, ANDERSON & CITKOWSKI, P.C, PO

NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT: 2162

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A number of human disorders are characterized by degeneration or loss of specific cells, resulting in pathology associated with reduction or absence of cell function. Such diseases include neurodegenerative diseases and diabetes. Methods are described for obtaining a substantially homogeneous population of undifferentiated human embryonic stem cells including incubating a population of human embryonic stem cells with an amount of a selection agent. The selection agent is effective to reduce or eliminate differentiated embryonic stem cells from the population of cells such that a substantially homogeneous population of undifferentiated human embryonic stem cells is obtained. The substantially homogeneous population of undifferentiated embryonic stem cells may be produced without use of feeder cells.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 16 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2007:95153 USPATFULL

TITLE: Pharmaceutical formulations employing short-chain

sphingolipids and their use

Veldman, Robert J., Huizen, NETHERLANDS INVENTOR(S):

Van Blitterswijk, Wim J., Westzaan, NETHERLANDS

Verheij, Marcel, Lisse, NETHERLANDS Koning, Gerben A., Houten, NETHERLANDS

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2007082855	A1	20070412	
APPLICATION INFO.:	US 2004-579230	A1	20041111	(10)
	WO 2004-IB3886		20041111	
			20060928	PCT 371 date

NUMBER DATE

GB 2003-26642 20031114 GB 2003-26759 20031117 PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: NIXON & VANDERHYE, PC, 901 NORTH GLEBE ROAD, 11TH

FLOOR, ARLINGTON, VA, 22203, US

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 4 Drawing Page(s)

2321 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention pertains to pharmaceutical formulations which comprise (i) a drug (e.g., an amphiphilic drug) (e.g., an anthracycline) (e.g., doxorubicin) and (ii) a short-chain sphingolipid (e.g., a short-chain glycosphingolipid or a short-chain sphingomyelin) (e.g., N-octanoyl-glucosylceramide, referred to as C.sub.8-GlcCer) (e.g., N-hexanoyl-sphingomyelin, referred to herein as C.sub.6-SM), and which provide improved drug delivery and efficacy. The short-chain sphingolipidis selected from compounds of the following formula: ##STR1## wherein: R.sup.1 is independently: an O-linked saccharide group; or an O-linked polyhydric alcohol group; or: R.sup.1 is independently: an O-linked (optionally N-(C.sub.1-4alkyl)-substituted amino)-C.sub.1-6alkyl-phosphate group; or an O-linked (polyhydric alcohol-substituted)-C.sub.1-6alkyl-phosphate group; R.sup.2 is independently C.sub.3-9alkyl, and is independently unsubstituted or substituted; R.sup.3 is independently C.sub.7-19alkyl, and is independently unsubstituted or substituted; R.sup.4 is independently --H, --OH, or --O--C.sub.1-4alkyl; R.sup.N is independently --H or C.sub.1-4alkyl; the bond marked with an alpha (α) is independently a single bond or a double bond; if the bond marked with an alpha (α) is a double bond, then R.sup.5 is --H; if the bond marked with an alpha (α) is a single bond, then R.sup.5 is --H or --OH; the carbon atom marked (*) is independently in an R-configuration or an S-configuration; the carbon atom marked (**) is independently in an R-configuration or an S-configuration; and pharmaceutically acceptable salts, solvates, esters, ethers, chemically protected forms thereof. In one embodiment, the pharmaceutical formulation is a liposomal pharmaceutical formulation prepared using a mixture of lipids comprising, at least, vesicle-forming lipids (e.g., phospholipids) (e.g., phosphatidylcholines) (e.g., fully hydrogenated soy phosphatidylcholine (HSPC)) (e.g., dipalmitoyl-phosphatidylcholine (DPPC)) and said short-chain sphingolipid, and optionally cholesterol and optionally a vesicle-forming lipid which is derivatized with a polymer chain (e.g., a phosphatidylethanolamine (PE) which is derivatized with polyethyleneglycol (PEG)) (e.g., N-(carbonylmethoxypolyethylene glycol 2000)-1,2-distearoyl-sn-glycero-3phosphoethanolamine sodium salt (MPEG2000-DSPE). The present invention also pertains to methods for the preparation and use of such

formulations.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 17 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2006:301138 USPATFULL

Nanoparticulate delivery systems for treating TITLE:

multi-drug resistance

INVENTOR(S): Amiji, Mansoor M., Attleboro, MA, UNITED STATES

Shenoy, Dinesh B., Boston, MA, UNITED STATES

Vlerken, Lilian van, Brookline, MA, UNITED STATES

NUMBER KIND DATE ______ US 2006257493 A1 20061116 US 2006-413067 A1 20060427 (11) PATENT INFORMATION: APPLICATION INFO.:

> NUMBER DATE _____

US 2005-675837P 20050428 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WEINGARTEN, SCHURGIN, GAGNEBIN & LEBOVICI LLP, TEN POST

OFFICE SQUARE, BOSTON, MA, 02109, US

NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 3 Drawing Page(s)
741

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

An encapsulated delivery system, and, in particular, a nanoparticulate delivery system representing a qualitatively different approach to overcoming multi-drug resistance while simultaneously administering the chosen drug treatment to a patient, e.g., in a site-specific manner, is disclosed. A composition according to the invention includes a therapeutically effective amount of one or more multi-drug resistance reversing agents selected from the group consisting of ceramide and ceramide modulators; and a therapeutically effective amount of a therapeutic agent, wherein the therapeutic agent is different from the one or more multi-drug resistance reversing agents, and the one or more multi-drug resistance reversing agents and the therapeutic agent are encapsulated, preferably co-encapsulated, in a biocompatible, biodegradable delivery vehicle for delivery to a patient in need of treatment, for example, for specific localization at, or higher probability of delivery to, a treatment site in a patient administered the composition. Preferably, the one or more multi-drug resistance reversing agents are ceramide, paclitaxel or tamoxifen.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 18 OF 22 USPATFULL on STN

2006:70187 USPATFULL ACCESSION NUMBER:

TITLE: Combinations of ceramide and chemotherapeutic

agents for inducing tumor cell death

Wanebo, Harold J., East Greenwich, RI, UNITED STATES Mehta, Shashikant, Warwick, RI, UNITED STATES INVENTOR(S):

PATENT ASSIGNEE(S): Roger Williams Hospital, Providence, RI, UNITED STATES

(U.S. corporation)

			NUMBER	KIND	DATE
PATENT	INFORMATION:	US	7015251	B1	20060321
		WO	2000059517		20001012

US 2000-958453 APPLICATION INFO.: 20000407 (9)

WO 2000-US9440 20000407

20020424 PCT 371 date

Continuation-in-part of Ser. No. US 1999-287884, filed RELATED APPLN. INFO.:

on 7 Apr 1999, ABANDONED

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

PRIMARY EXAMINER: Cook, Rebecca

LEGAL REPRESENTATIVE: White, Esq., John P., Cooper & Dunham LLP

NUMBER OF CLAIMS: 14 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 47 Drawing Figure(s); 24 Drawing Page(s)

LINE COUNT: 2051

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a method for increasing apoptosis in tumor cells and a method of decreasing a size of a tumor , said methods comprising contacting the tumor cells with: a) an effective amount of at least one antitumor chemotherapeutic agent and b) an effective amount of a ceramide, sequentially or concomitantly, wherein the apoptosis induced by the combination of the antitumor chemotherapeutic agent and the ceramide is greater than the apoptosis induced by contact of the tumor cells with either the antitumor chemotherapeutic agent alone or the ceramide alone. This invention also provides a method of treating cancer in a subject which comprises a method according to either of the above-described methods. This invention provides a method for treating cancer in a subject comprising administering to the subject an effective amount of at least one antitumor chemotherapeutic agent and an effective amount of at least one ceramide, sequentially or concomitantly. This invention provides a pharmaceutical composition comprising at least one antitumor chemotherapeutic agent in an amount effective to induce apoptosis of tumor cells and at least one ceramide in an amount effective to induce apoptosis of tumor cells and a pharmaceutically acceptable carrier.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 19 OF 22 USPATFULL on STN

INVENTOR(S):

ACCESSION NUMBER: 2005:30390 USPATFULL

TITLE: Method and system for systemic delivery of growth

> arresting, lipid-derived bioactive compounds Kester, Mark, Harrisburg, PA, UNITED STATES Stover, Thomas, Hershey, PA, UNITED STATES

Lowe, Tao, Hershey, PA, UNITED STATES

Adair, James, UNITED STATES

Kim, Young Shin, Hershey, PA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005025820	A1	20050203	
APPLICATION INFO.:	US 2004-835520	A1	20040426	(10)

			NUMBER	DATE	
PRIORITY	INFORMATION:	US	2003-465938P	20030425	(60)
		US	2003-465937P	20030428	(60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Barbara E. Johnson, WEBB ZIESENHEIM LOGSDON ORKIN &

HANSON, P.C., 700 Koppers Building, 436 Seventh Avenue,

Pittsburgh, PA, 15219-1818

NUMBER OF CLAIMS: 77 1 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 20 Drawing Page(s) LINE COUNT: 1954

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A system and method for optimizing the systemic delivery of growth-arresting lipid-derived bioactive drugs or gene therapy agents to an animal or human in need of such agents utilizing nanoscale assembly systems, such as liposomes, resorbable and non-aggregating nanoparticle dispersions, metal or semiconductor nanoparticles, or polymeric materials such as dendrimers or hydrogels, each of which exhibit improved lipid solubility, cell permeability, an increased circulation half life and pharmacokinetic profile with improved tumor or vascular targeting.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ANSWER 20 OF 22 USPATFULL on STN

ACCESSION NUMBER: 2003:232006 USPATFULL

Ceramide kinase and DNA encoding it TITLE:

Sugiura, Masako, Tokyo, JAPAN INVENTOR(S): Kono, Keita, Kawasaki-shi, JAPAN Kohama, Takafumi, Tokyo, JAPAN

SANKYO COMPANY, LIMITED, Tokyo, JAPAN (non-U.S. PATENT ASSIGNEE(S):

corporation)

NUMBER KIND DATE PATENT INFORMATION: ______ US 2003162206 A1 20030828 US 2002-315597 A1 20021210 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2001-JP4889, filed

on 11 Jun 2001, UNKNOWN

NUMBER DATE _____ JP 2000-178039 20000614

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: FRISHAUF, HOLTZ, GOODMAN & CHICK, PC, 767 THIRD AVENUE,

25TH FLOOR, NEW YORK, NY, 10017-2023

75 1 NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT: 1913

PRIORITY INFORMATION:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A protein having ceramide kinase activity which can be a target for a prophylactic or therapeutic medicament against neuronal disease, inflammation, HIV infection, type 2 diabetes mellitus, obesity, septicemia, arteriosclerosis and cancer. Specifically, a protein which comprises an amino acid sequence shown in the amino acid numbers 1-537 of SEQ ID Number 2 of the Sequence Listing, a DNA which encodes the protein, a recombinant vector comprising the DNA, a host cell transformed with the recombinant vector and a method for producing the protein. By using the method of the present invention, a compound is provided having a specifically activating or inhibiting activity to ceramide kinase and is useful as a medicament for treating a neuronal disorder, an anti-inflammatory medicament, a medicament for treating HIV infection, an anti-type 2 diabetes mellitus medicament, an anti-obesity medicament, an anti-septicemia medicament, an anti-arteriosclerosis medicament and an anticancer medicament.

L5 ANSWER 21 OF 22 USPATFULL on STN

ACCESSION NUMBER: 97:99045 USPATFULL

TITLE: Liposomal ceramide-related liposomes and the

therapeutic use thereof

INVENTOR(S): Wei, Yong, Branchburg, NJ, United States

Mayhew, Eric, Monmouth Junction, NJ, United States

Ahmad, Imran, Plainsboro, NJ, United States Janoff, Andrew S., Yardley, PA, United States

PATENT ASSIGNEE(S): The Lipsome Company, Inc., Princeton, NJ, United States

(U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5681589 19971028
APPLICATION INFO.: US 1995-545164 19951019 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-383291, filed on 2 Feb

1995 which is a continuation-in-part of Ser. No. US $\,$

1994-190295, filed on 2 Feb 1994, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Kishore, Gollamudi S. LEGAL REPRESENTATIVE: Rubin, Kenneth B.

NUMBER OF CLAIMS: 15 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 21 Drawing Figure(s); 21 Drawing Page(s)

LINE COUNT: 1282

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a compound having the formula R.sup.1 -Y.sup.1 --CHZ.sup.1 -CH(NY.sup.2 Y.sup.3)--CH.sub.2 -Z.sup.2, wherein: R.sup.1 is a straight-chained alkyl, alkenyl or alkynyl group having from 8 to 19 carbon atoms in the aliphatic chain; Y.sup.1 is --CH.dbd.CH--, --C.tbd.C-- or --CH(OH)CH(OH)--; Z.sup.1 is OH or a conversion-inhibiting group; Z.sup.2 is a conversion-inhibiting group; Y.sup.2 is H, a phenyl group, an alkyl-substituted phenyl group having from 1 to about 6 carbons in the alkyl chain, or an alkyl chain having from 1 to 6 carbons; Y.sup.3 is H or a group having the formula --C(O)R.sup.2 or --S(O).sub.2 R.sup.2; R.sup.2 is a straight-chained alkyl, alkenyl or alkynyl group having from 1 to 23 carbon atoms in the chain; and when Z.sup.2 is an amino, R.sup.2 is an aliphatic chain having from 1 to 9 or from 19 to 23 carbon atoms in the aliphatic chain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 22 OF 22 USPATFULL on STN

ACCESSION NUMBER: 97:94269 USPATFULL

TITLE: Methods of treatment using pharmaceutically active

ceramide-related compositions

INVENTOR(S): Wei, Yong, Branchburg, NJ, United States

Mayhew, Eric, Monmouth Junction, NJ, United States

Ahmad, Imran, Plainsboro, NJ, United States Janoff, Andrew S., Yardley, PA, United States

PATENT ASSIGNEE(S): The Liposome Company, Inc., Princeton, NJ, United

States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5677337 19971014 APPLICATION INFO.: US 1995-547688 19951019 (8)

RELATED APPLN. INFO.: Division of Ser. No. US 1995-383291, filed on 2 Feb 1995, now patented, Pat. No. US 5631394 which is a

continuation-in-part of Ser. No. US 1994-190295, filed

on 2 Feb 1994, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Kishore, Gollamudi S. LEGAL REPRESENTATIVE: Rubin, Kenneth B.

NUMBER OF CLAIMS: 17 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 21 Drawing Figure(s); 21 Drawing Page(s)

LINE COUNT: 1302

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

This invention provides a compound having the formula R.sup.1 --Y.sup.1 --CHZ.sup.1 --CH(NY.sup.2 Y.sup.3)--CH.sub.2 --Z.sup.2, wherein: R.sup.1 is a straight-chained alkyl, alkenyl or alkynyl group having from 8 to 19 carbon atoms in the aliphatic chain; Y.sup.1 is --CH.dbd.CH--, --C.tbd.C-- or --CH(OH)CH(OH)--; Z.sup.1 is OH or a conversion-inhibiting group; Z.sup.2 is a conversion-inhibiting group; Y.sup.2 is H, a phenyl group, an alkyl-substituted phenyl group having from 1 to about 6 carbons in the alkyl chain, or an alkyl chain having from 1 to 6 carbons; Y.sup.3 is H or a group having the formula --C(O)R.sup.2 or --S(O).sub.2 R.sup.2; R.sup.2 is a straight-chained alkyl, alkenyl or alkynyl group having from 1 to 23 carbon atoms in the chain; and when Z.sup.2 is an amino, R.sup.2 is an aliphatic chain having from 1 to 9 or from 19 to 23 carbon atoms in the aliphatic chain.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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(FILE 'HOME' ENTERED AT 10:16:05 ON 12 FEB 2008)

FILE 'REGISTRY' ENTERED AT 10:16:44 ON 12 FEB 2008

E "N-HEXANOYL-D-SPHINGOSINE"/CN 25

L1 1 S E1

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:18:02 ON 12 FEB 2008

L2 240 S L1

L3 15 S L2 AND (PACLITAXEL OR TAXOL) L4 78 S L2 AND (?CANCER? OR ?TUMOR?)

L5 22 S L4 AND COMBINATION?

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 130.28 138.56 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE -19.20-19.20

STN INTERNATIONAL LOGOFF AT 10:24:56 ON 12 FEB 2008